AMENDMENT TO THE CLAIMS

The present document adds claims 48-51. According to 37 C.F.R. § 1.121(c), after entry of the present amendment, the status of the claims in the case is as follows:

Claims 1 and 2 Canceled

3. (Previously Presented) The method of claim 5, wherein said immunoconjugate binds to VEGF bound to the VEGF receptor VEGFR1 expressed by endothelial cells of the vasculature of said vascularized tumor.

4. (Previously Presented) The method of claim 5, wherein said immunoconjugate binds to VEGF bound within the stroma of said vascularized tumor.

5. (Previously Presented) A method for treating cancer, comprising administering to an animal that has a vascularized solid tumor, a metastatic tumor or metastases from a primary tumor, a therapeutically effective amount of:

(a) a first pharmaceutical composition comprising at least a first immunoconjugate that comprises at least a first cleavage agent or enzyme operatively attached to at least a first anti-VEGF antibody, or antigen-binding fragment thereof, that binds to substantially the same epitope as the monoclonal antibody 2C3 (ATCC PTA 1595), thereby localizing said immunoconjugate to the vasculature or stroma of said vascularized solid tumor; and

(b) subsequently administering to said animal a second composition that comprises at least one substantially inactive prodrug that is cleaved by the cleavage agent or

enzyme attached to said antibody in said first pharmaceutical composition, thereby releasing a substantially active drug specifically within the vasculature or stroma of said vascularized solid tumor.

6. (Original) The method of claim 5, wherein said at least a first antibody of said immunoconjugate is a monoclonal antibody or an antigen-binding fragment thereof.

7. (Original) The method of claim 5, wherein said at least a first antibody of said immunoconjugate is an scFv, Fv, Fab', Fab, diabody, linear antibody or $F(ab')_2$ antigen-binding fragment of an antibody.

8. (Original) The method of claim 5, wherein said at least a first antibody of said immunoconjugate is a human, humanized or part-human antibody or antigen-binding fragment thereof.

9. (Original) The method of claim 5, wherein said at least a first antibody of said immunoconjugate is a chimeric antibody or a recombinant antibody.

10. (Original) The method of claim 5, wherein said at least a first antibody of said immunoconjugate comprises at least a first variable region that includes an amino acid sequence region having the amino acid sequence of SEQ ID NO:7 or SEQ ID NO:9.

11. (Original) The method of claim 5, wherein said at least a first antibody of said immunoconjugate is the monoclonal antibody 2C3 (ATCC PTA 1595).

12. (Previously Presented) The method of claim 5, wherein said immunoconjugate comprises said at least a first antibody operatively attached to two or more cleavage agents or enzymes.

Claims 13-24 Canceled

25. (Previously Presented) The method of claim 5, wherein said immunoconjugate comprises said at least a first antibody operatively attached to said at least a first cleavage agent or enzyme as a fusion protein prepared by expressing a recombinant vector that comprises, in the same reading frame, a DNA segment encoding said antibody operatively linked to a DNA segment encoding said cleavage agent or enzyme.

Claims 26-28 Canceled

29. (Previously Presented) The method of claim 5, wherein said first pharmaceutical composition is administered to said animal intravenously.

30. (Original) The method of claim 5, further comprising subjecting said animal to radiotherapy.

31. (Original) The method of claim 5, further comprising administering to said animal a therapeutically effective amount of at least a second anti-cancer agent.

Claims 32 and 33 Canceled

34. (Previously Presented) The method of claim 31, wherein said at least a second anti-cancer agent is a chemotherapeutic agent, radiotherapeutic agent, anti-angiogenic agent, apoptosis-inducing agent, steroid, antimetabolite, anthracycline, vinca alkaloid, antibiotic, cytokine, alkylating agent, coagulant or anti-tubulin drug or tumor-targeted form thereof.

35. (Previously Presented) The method of claim 34, wherein said at least a second anti-cancer agent is angiopoietin-2, endostatin, angiostatin, vasculostatin, canstatin, maspin, colchicine, taxol, vinblastine, vincristine, vindescine, a combretastatin, or tumor-targeted form thereof.

36. (Original) The method of claim 31, wherein said at least a second anti-cancer agent is a targeting agent-therapeutic agent construct comprising a therapeutic agent operatively linked to at least a first targeting region that binds to an accessible component of a tumor cell or tumor stroma or to a surface-expressed, surface-accessible, surface-localized, cytokine-inducible or coagulant-inducible component of tumor vasculature or intratumoral vasculature.

37. (Previously Presented) The method of claim 36, wherein said at least a first targeting region is operatively linked to a cytotoxic, cytostatic or anticellular agent, anti-angiogenic agent, apoptosis-inducing agent or anti-tubulin drug.

38. (Original) The method of claim 36, wherein said at least a first targeting region is operatively linked to Tissue Factor, truncated Tissue Factor or a Tissue Factor derivative or to an antibody, or antigen-binding fragment thereof, that binds to Tissue Factor, truncated Tissue Factor or a Tissue Factor derivative.

39. (Previously Presented) The method of claim 36, wherein said at least a first targeting region is operatively linked to a plant-, fungus- or bacteria-derived toxin.

Claim 40 Canceled

41. (Previously Presented) The method of claim 5, wherein said at least a first cleavage agent or enzyme and said at least one substantially inactive prodrug are operably matched agents selected from the groups consisting of:

(a) alkaline phosphatase, arylsulfatase, serratia protease, thermolysin, subtilisin, a carboxypeptidase, a cathepsin, D-alanylcarboxypeptidase, β-galactosidase, neuraminidase, β-lactamase, penicillin amidase and cytosine deaminase; and

(b) a phosphate-containing prodrug, sulfate-containing prodrug, peptide-based prodrug, D-amino acid-modified prodrug, glycosylated prodrug, β-lactam-containing prodrug, optionally substituted phenoxyacetamide- or phenylacetamide-containing prodrug and 5-fluorocytosine.

42. (Original) The method of claim 5, wherein said animal is a human patient.

Claims 43-45 Canceled

46. (Previously Presented) A method for treating cancer, comprising administering to an animal that has a vascularized solid tumor:

(a) a first composition comprising at least a first immunoconjugate that comprises at least a first cleavage agent or enzyme operatively attached to at least a first anti-VEGF antibody, or antigen-binding fragment thereof, that effectively competes with the monoclonal antibody 2C3 (ATCC PTA 1595) for binding to VEGF, thereby localizing said immunoconjugate to the vasculature or stroma of said vascularized solid tumor; and

(b) subsequently administering to said animal a second composition that comprises at least one substantially inactive prodrug that is cleaved by the cleavage agent or enzyme attached to said antibody in said first composition, thereby releasing a substantially active drug specifically within the vasculature or stroma of said vascularized solid tumor.

47. (Previously Presented) The method of claim 5, wherein said immunoconjugate localizes to the vasculature and stroma of said vascularized tumor.

48. (New) The method of claim 5, wherein said at least a first antibody, or antigen-binding fragment thereof, of said immunoconjugate comprises at least a first variable region that includes an amino acid sequence region having the amino acid sequence of SEQ ID NO:7 or SEQ ID NO:9.

49. (New) A method for treating cancer, comprising administering to an animal that has a vascularized solid tumor, a metastatic tumor or metastases from a primary tumor, a therapeutically effective amount of:

(a) a first pharmaceutical composition comprising at least a first immunoconjugate that comprises at least a first cleavage agent or enzyme operatively attached to at least a first anti-VEGF antibody, or antigen-binding fragment thereof, that binds to substantially the same epitope as the monoclonal antibody 2C3 (ATCC PTA 1595), thereby localizing said immunoconjugate to the vasculature or stroma of said vascularized solid tumor; wherein said antibody, or antigen-binding fragment thereof, comprises at least a first variable region that includes an amino acid sequence region having the amino acid sequence of SEQ ID NO:7 or SEQ ID NO:9; and

(b) subsequently administering to said animal a second composition that comprises at least one substantially inactive prodrug that is cleaved by the cleavage agent or enzyme attached to said antibody in said first pharmaceutical composition, thereby releasing a substantially active drug specifically within the vasculature or stroma of said vascularized solid tumor.

50. (New) A method for treating cancer, comprising administering to an animal that has a vascularized solid tumor, a metastatic tumor or metastases from a primary tumor, a therapeutically effective amount of:

(a) a first pharmaceutical composition comprising at least a first immunoconjugate that comprises at least a first cleavage agent or enzyme operatively attached to at least a first anti-VEGF antibody, or antigen-binding fragment thereof, that binds to substantially the same epitope as the monoclonal antibody 2C3 (ATCC PTA 1595), thereby localizing said immunoconjugate to the vasculature and stroma of said vascularized solid tumor; and

(b) subsequently administering to said animal a second composition that comprises at least one substantially inactive prodrug that is cleaved by the cleavage agent or enzyme attached to said antibody in said first pharmaceutical composition, thereby releasing a substantially active drug specifically within the vasculature and stroma of said vascularized solid tumor.

51. (New) A method for treating cancer, comprising administering to an animal that has a vascularized solid tumor, a metastatic tumor or metastases from a primary tumor, a therapeutically effective amount of:

(a) a first pharmaceutical composition comprising at least a first immunoconjugate that comprises at least a first cleavage agent or enzyme operatively attached to at least a first anti-VEGF antibody, or antigen-binding fragment thereof, that binds to substantially the same epitope as the monoclonal antibody 2C3 (ATCC PTA 1595); wherein said immunoconjugate binds to VEGF bound to the VEGF receptor VEGFR1 expressed by endothelial cells of the vasculature of said vascularized tumor, thereby localizing said immunoconjugate to the tumor vasculature; and

(b) subsequently administering to said animal a second composition that comprises at least one substantially inactive prodrug that is cleaved by the cleavage agent or enzyme attached to said antibody in said first pharmaceutical composition, thereby releasing a substantially active drug specifically within the vasculature of said vascularized solid tumor.